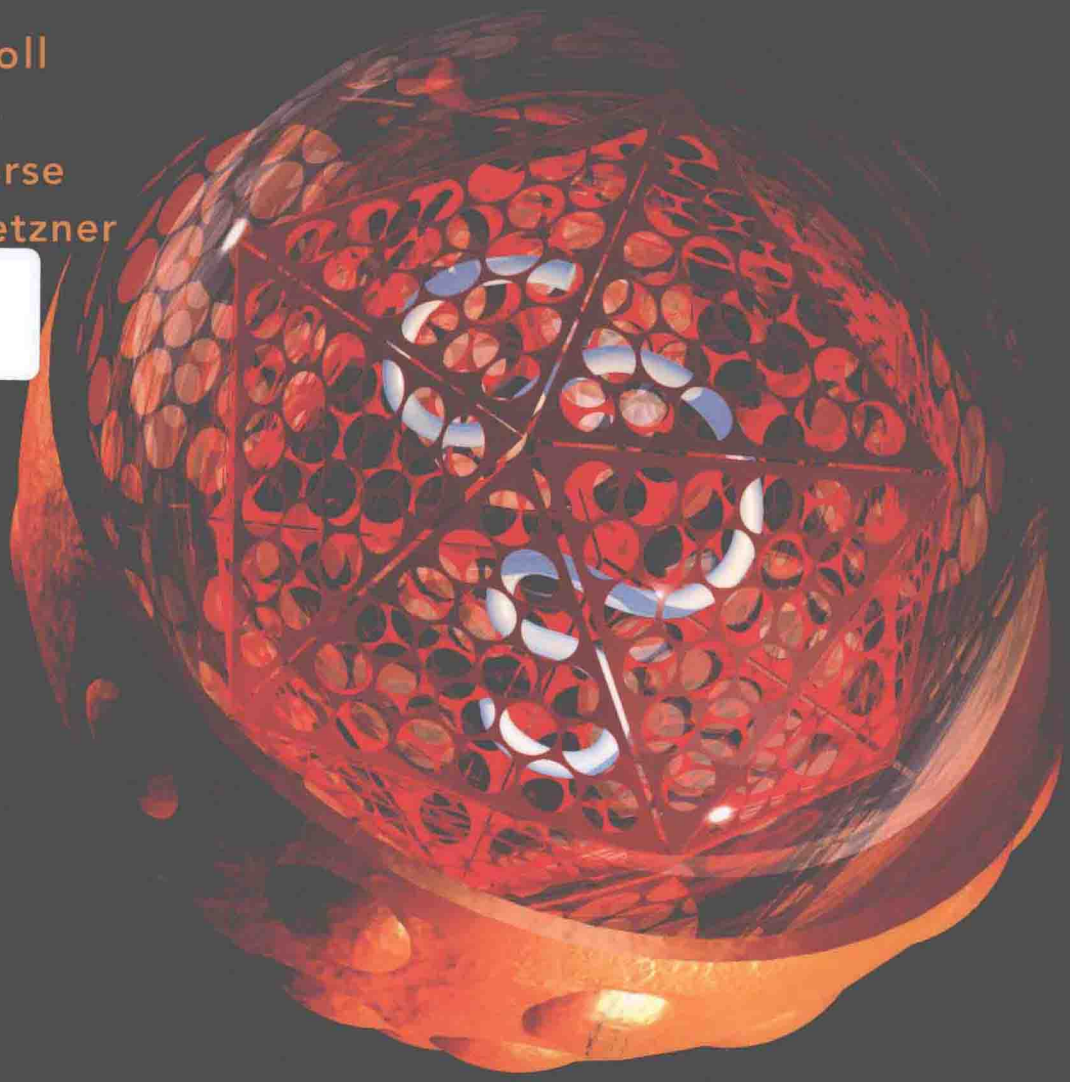
Geo. F. Brooks
Karen C. Carroll
Janet S. Butel
Stephen A. Morse
Timothy A. Mietzner



Jawetz, Melnick & Adelberg's

MEDICAL MICROBIOLOGY

26th Edition

Mc Graw Hill LANGE®

a LANGE medical book

Jawetz, Melnick, & Adelberg's Medical Microbiology

Twenty-Sixth Edition

Geo. F. Brooks, MD
Professor of Laboratory Medicine
and Microbiology and Immunology
Chief, Microbiology Section
Clinical Laboratories
University of California
San Francisco, California

Karen C. Carroll, MD
Professor of Pathology
The Johns Hopkins University School of Medicine
Director, Division of Medical Microbiology
The Johns Hopkins Hospital
Baltimore, Maryland

Janet S. Butel, PhD
Distinguished Service Professor
Chair, Department of Molecular Virology and
Microbiology
Baylor College of Medicine
Houston, Texas

Stephen A. Morse, PhD
Associate Director for Environmental Microbiology
Division of Foodborne, Waterborne, and
Environmental Diseases
National Center for Emerging and Zoonotic
Infectious Diseases
Centers for Disease Control and Prevention
Atlanta, Georgia

Timothy A. Mietzner, PhD
Associate Professor
Department of Microbiology and Molecular
Genetics
University of Pittsburgh School of Medicine
Pittsburgh
Adjunct Associate Professor of Microbiology
Arizona School of Dentistry and Oral Health
Mesa, Arizona

Mc Graw Hill Medical

New York Chicago San Francisco Lisbon London Madrid Mexico City
Milan New Delhi San Juan Seoul Singapore Sydney Toronto

The McGraw-Hill Companies

Jawetz, Melnick, & Adelberg's Medical Microbiology, Twenty-Sixth Edition

1 2 3 4 5 6 7 8 9 0 DOW/DOW 18 17 16 15 14 13 12

ISBN 978-0-07-179031-4
MHID 0-07-179031-4
ISSN 1054-2744

Notice

Medicine is an ever-changing science. As new research and clinical experience broaden our knowledge, changes in treatment and drug therapy are required. The authors and the publisher of this work have checked with sources believed to be reliable in their efforts to provide information that is complete and generally in accord with the standards accepted at the time of publication. However, in view of the possibility of human error or changes in medical sciences, neither the authors nor the publisher nor any other party who has been involved in the preparation or publication of this work warrants that the information contained herein is in every respect accurate or complete, and they disclaim all responsibility for any errors or omissions or for the results obtained from use of the information contained in this work. Readers are encouraged to confirm the information contained herein with other sources. For example and in particular, readers are advised to check the product information sheet included in the package of each drug they plan to administer to be certain that the information contained in this work is accurate and that changes have not been made in the recommended dose or in the contraindications for administration. This recommendation is of particular importance in connection with new or infrequently used drugs.

The book was set in minion pro by Cenveo Publisher Services.
The editors were Michael Weitz and Christie Naglieri.
The production supervisor was Catherine Saggese.
Project management was provided by Sheena Uprety, Cenveo Publisher Services.
The designer was Elise Lansdon.
Cover photo: Virus of hepatitis C. (c) BSIP/Corbis.
RR Donnelley was the printer and binder.

SELECTED MEDICALLY IMPORTANT MICROORGANISMS

I. BACTERIA

AEROBIC AND FACULTATIVE BACTERIA

GRAM-POSITIVE COCCI

Catalase-Positive

Staphylococcus aureus
Staphylococcus epidermidis
Staphylococcus intermedius
Staphylococcus lugdunensis
Staphylococcus saprophyticus
Staphylococcus species

Catalase-Negative

Aerococcus species
Enterococcus faecalis
Enterococcus faecium
Enterococcus species
Gemella species
Lactococcus species
Leuconostoc species
Pediococcus species
Streptococcus agalactiae (Group B)
Streptococcus canis (Group G)
Streptococcus gallolyticus (Group D, formerly *S. bovis*)
Streptococcus infantarius (Group D, formerly *S. bovis*)
Streptococcus pneumoniae
Streptococcus pyogenes (Group A)
Viridans group streptococci
Streptococcus anginosus
Streptococcus constellatus
Streptococcus intermedius
Streptococcus mitis
Streptococcus mutans
Streptococcus salivarius
Streptococcus sanguis
Abiotrophia species (nutritionally variant streptococci)
Granulicatella species (nutritionally variant streptococci)

GRAM-NEGATIVE COCCI

Moraxella catarrhalis
Neisseria gonorrhoeae
Neisseria meningitidis
Neisseria species

GRAM-POSITIVE BACILLI

Arcanobacterium species
Bacillus anthracis
Bacillus cereus
Corynebacterium diphtheriae
Corynebacterium jeikeium
Corynebacterium species
Corynebacterium urealyticum
Erysipelothrix rhusiopathiae
Gardnerella vaginalis
Gordonia species
Listeria monocytogenes
Mycobacterium abscessus
Mycobacterium avium
Mycobacterium bovis
Mycobacterium chelonae
Mycobacterium fortuitum
Mycobacterium intracellulare
Mycobacterium kansasii
Mycobacterium leprae
Mycobacterium marinum
Mycobacterium tuberculosis
Mycobacterium species
Nocardia asteroides
Rhodococcus equi
Tropheryma whippeli
Tsukamurella species

GRAM-NEGATIVE BACILLI

Enterobacteriaceae

Citrobacter freundii
Citrobacter koseri
Citrobacter species
Cronobacter sakazakii
Edwardsiella tarda
Enterobacter aerogenes
Enterobacter cloacae
Escherichia coli
Escherichia species
Klebsiella oxytoca
Klebsiella granulomatis
Klebsiella pneumoniae
Klebsiella pneumoniae subspecies rhinocscleromatis
Morganella morganii
Plesiomonas shigelloides
Proteus mirabilis
Proteus vulgaris
Providencia alcalifaciens
Providencia rettgeri
Providencia stuartti
Salmonella Choleraesuis
Salmonella Paratyphi A
Salmonella Paratyphi B
Salmonella Typhi
Salmonella species
Serratia liquefaciens
Serratia marcescens
Shigella boydii
Shigella dysenteriae
Shigella flexneri
Shigella sonnei
Yersinia enterocolitica
Yersinia pestis
Yersinia pseudotuberculosis

Nonenterobacteriaceae—Fermentative Bacilli

Aeromonas caviae
Aeromonas hydrophila
Aeromonas species
Aeromonas veronii biovar sobria
Pasteurella multocida
Vibrio cholerae
Vibrio parahaemolyticus
Vibrio species
Vibrio vulnificus

Nonenterobacteriaceae—Nonfermentative Bacilli

Acinetobacter species
Alcaligenes species
Brevundimonas species
Burkholderia cepacia
Burkholderia mallei
Burkholderia pseudomallei
Chryseobacterium species
Comamonas species
Eikenella corrodens
Moraxella species
Pseudomonas aeruginosa
Pseudomonas fluorescens
Pseudomonas species
Ralstonia pickettii
Roseomonas species
Shewanella putrefaciens
Sphingobacterium species
Sphingomonas species
Stenotrophomonas maltophilia

OTHER GRAM-NEGATIVE BACILLI AND COCCOBACILLI

Aggregatibacter (Actinobacillus) actinomycetemcomitans
Aggregatibacter (Haemophilus) aphrophilus
Arcobacter species
Bartonella bacilliformis
Bartonella henselae
Bartonella species
Bordetella bronchiseptica
Bordetella parapertussis
Bordetella pertussis
Bordetella species
Brucella melitensis
Brucella species
Campylobacter fetus
Campylobacter jejuni
Campylobacter species
Capnocytophaga species
Cardiobacterium hominis
Chlamydophila pneumoniae
Chlamydophila psittaci
Chlamydia trachomatis
Ehrlichia chaffeensis
Francisella tularensis
Haemophilus aegyptius
Haemophilus ducreyi
Haemophilus influenzae
Haemophilus parainfluenzae
Haemophilus species
Helicobacter pylori
Kingella kingae
Legionella micdadei
Legionella pneumophila
Legionella species
Orientia tsutsugamushi
Streptobacillus moniliformis

MYCOPLASMAS

Mycoplasma genitalium
Mycoplasma hominis
Mycoplasma pneumoniae
Mycoplasma species
Ureaplasma urealyticum

RICKETTSIA AND RELATED ORGANISMS

Anaplasma

Ehrlichia

Ehrlichia chaffeensis
Ehrlichia ewingii

Rickettsia

Rickettsia akari
Rickettsia conorii
Rickettsia mooseri
Rickettsia prowazekii
Rickettsia rickettsii

SPIRAL ORGANISMS

Borrelia burgdorferi
Borrelia recurrentis
Leptospira interrogans
Treponema pallidum

ANAEROBIC BACTERIA

GRAM-NEGATIVE BACILLI

Bacteroides fragilis group
Bacteroides ovatus
B distasonis
B thetaiotamicron
B vulgatus
Bacteroides species
Fusobacterium necrophorum
Fusobacterium nucleatum
Mobiluncus species

(Continued on inside back cover)

Preface

The twenty-sixth edition of *Jawetz, Melnick, & Adelberg's Medical Microbiology* remains true to the goals of the first edition published in 1954 "to provide a brief, accurate and up-to-date presentation of those aspects of medical microbiology that are of particular significance to the fields of clinical infections and chemotherapy." The 26th edition has included the following new features!

- Addition of concept checks after major sections within chapters.
- Chapter Summaries at the end of each chapter.
- Increased number of new and revised review questions.
- Full color photographs and photomicrographs of the previous edition.
- All chapters have been revised extensively consistent with the tremendous expansion of medical knowledge afforded by molecular mechanisms, advances in our understanding of microbial pathogenesis and the discovery of novel pathogens.

New also to this edition is Barbara Detrick, PhD, Professor in the Division of Clinical Immunology in the Department of Pathology at the Johns Hopkins University School of Medicine. Dr. Detrick's extensive expertise in clinical immunology, and in particular the role of cytokines in health and disease, will add significantly to the current and future editions and we welcome her participation.

The authors hope that the changes to this edition will be helpful to the student of microbiology.

Geo. F. Brooks
San Francisco, California

Karen C. Carroll
Baltimore, Maryland

Janet S. Butel
Houston, Texas

Stephen A. Morse
Atlanta, Georgia

Timothy A. Meitzner
Mesa, Arizona

November 2012

Contents

SECTION II

IMMUNOLOGY 123

Barbara Detrick, PhD

SECTION III

BACTERIOLOGY 149

Karen C. Carroll, MD

SECTION I FUNDAMENTALS OF MICROBIOLOGY

CHAPTER 1

The Science of Microbiology

INTRODUCTION

Microbiology is the study of microorganisms, a large and diverse group of microscopic organisms that exist as single cells or cell clusters; it also includes viruses, which are microscopic but not cellular. Microorganisms have a tremendous impact on all life and the physical and chemical makeup of our planet. They are responsible for cycling the chemical elements essential for life, including carbon, nitrogen, sulfur, hydrogen, and oxygen; more photosynthesis is carried out by microorganisms than by green plants. Furthermore, there are 100 million times as many bacteria in the oceans (13×10^{28}) as there are stars in the known universe. The rate of viral infections in the oceans is about 1×10^{23} infections per second, and these infections remove 20–40% of all bacterial cells each day. It has been estimated that 5×10^{30} microbial cells exist on earth; excluding cellulose, these cells constitute about 90% of the biomass of the entire biosphere. Humans also have an intimate relationship with microorganisms; more than 90% of the cells in our bodies are microbes. The bacteria present in the average human gut weigh about 1 kg, and a human adult will excrete his or her own weight in fecal bacteria each year. The number of genes contained within this gut flora outnumber that contained within our genome 150-fold, and even in our own genome, 8% of the DNA is derived from remnants of viral genomes.

BIOLOGIC PRINCIPLES ILLUSTRATED BY MICROBIOLOGY

Nowhere is **biologic diversity** demonstrated more dramatically than by microorganisms, creatures that are not directly visible to the unaided eye. In form and function, be it biochemical property or genetic mechanism, analysis of microorganisms takes us to the limits of biologic understanding. Thus, the need for **originality**—one test of the merit of a scientific **hypothesis**—can be fully met in microbiology. A useful hypothesis should provide a basis for **generalization**, and microbial diversity provides an arena in which this challenge is ever present.

Prediction, the practical outgrowth of science, is a product created by a blend of technique and theory. **Biochemistry**, **molecular biology**, and **genetics** provide the tools required for analysis of microorganisms. **Microbiology**, in turn, extends the horizons of these scientific disciplines. A biologist might describe such an exchange as **mutualism**, that is, one that benefits all of the contributing parties. Lichens are an example of microbial mutualism. Lichens consist of a fungus and phototropic partner, either an alga (a eukaryote) or a cyanobacterium (a prokaryote). The phototropic component is the primary producer, and the fungus provides the phototroph with an anchor and protection from the elements. In biology, mutualism is called **symbiosis**, a continuing association of different organisms. If the exchange operates primarily to the benefit of one party, the association is described as **parasitism**, a relationship in which a **host** provides the primary benefit to the parasite. Isolation and characterization of a parasite—such as a pathogenic bacterium or virus—often require effective mimicry in the laboratory of the growth environment provided by host cells. This demand sometimes represents a major challenge to investigators.

The terms *mutualism*, *symbiosis*, and *parasitism* relate to the science of **ecology**, and the principles of environmental biology are implicit in microbiology. Microorganisms are

the products of **evolution**, the biologic consequence of **natural selection** operating on a vast array of genetically diverse organisms. It is useful to keep the complexity of natural history in mind before generalizing about microorganisms, the most heterogeneous subset of all living creatures.

A major biologic division separates the eukaryotes, organisms containing a membrane-bound nucleus, from prokaryotes, organisms in which DNA is not physically separated from the cytoplasm. As described in this chapter and in Chapter 2, further major distinctions can be made between eukaryotes and prokaryotes. Eukaryotes, for example, are distinguished by their relatively large size and by the presence of specialized membrane-bound organelles such as mitochondria.

As described more fully later in this chapter, eukaryotic microorganisms—or, phylogenetically speaking, the Eukarya—are unified by their distinct cell structure and phylogenetic history. Among the groups of eukaryotic microorganisms are the **algae**, the **protozoa**, the **fungi**, and the **slime molds**.

VIRUSES

The unique properties of viruses set them apart from living creatures. Viruses lack many of the attributes of cells, including the ability to replicate. Only when it infects a cell does a virus acquire the key attribute of a living system—reproduction. Viruses are known to infect all cells, including microbial cells. Recently, viruses called **virophages** have been discovered that infect other viruses. Host–virus interactions tend to be highly specific, and the biologic range of viruses mirrors the diversity of potential host cells. Further diversity of viruses is exhibited by their broad array of strategies for replication and survival.

Viral particles are generally small (eg, adenovirus is 90 nm) and consist of a nucleic acid molecule, either DNA or RNA, enclosed in a protein coat, or capsid (sometimes itself enclosed by an envelope of lipids, proteins, and carbohydrates). Proteins—frequently glycoproteins—in the capsid determine the specificity of interaction of a virus with its host cell. The capsid protects the nucleic acid and facilitates attachment and penetration of the host cell by the virus. Inside the cell, viral nucleic acid redirects the host's enzymatic machinery to functions associated with replication of the virus. In some cases, genetic information from the virus can be incorporated as DNA into a host chromosome. In other instances, the viral genetic information can serve as a basis for cellular manufacture and release of copies of the virus. This process calls for replication of the viral nucleic acid and production of specific viral proteins. **Maturation** consists of assembling newly synthesized nucleic acid and protein subunits into mature viral particles, which are then liberated into the extracellular environment. Some very small viruses require the assistance of another virus in the host cell for their duplication. The delta agent, also known as hepatitis D virus, is too small to code for even a single capsid protein and needs help from hepatitis B virus for transmission. Viruses are known to infect a wide variety of plant and animal hosts as well as protists, fungi, and bacteria. However, most viruses are able to infect specific types of cells of only one host species.

Some viruses are large and complex. For example, Mimivirus, a DNA virus infecting *Acanthamoeba*, a free-living soil ameba, has a diameter of 400–500 nm and a genome that encodes 979 proteins, including the first four aminoacyl tRNA synthetases ever found outside of cellular organisms and enzymes for polysaccharide biosynthesis. An even larger marine virus has recently been discovered (Megavirus); its genome (1,259,197-bp) encodes 1120 putative proteins and is larger than that of some bacteria (Table 7-1). Because of their large size, these viruses resemble bacteria when observed in stained preparations by light microscopy; however, they do not undergo cell division or contain ribosomes.

A number of transmissible plant diseases are caused by **viroids**—small, single-stranded, covalently closed circular RNA molecules existing as highly base-paired rodlike structures. They range in size from 246 to 375 nucleotides in length. The extracellular form of the viroid is naked RNA—there is no capsid of any kind. The RNA molecule contains no protein-encoding genes, and the viroid is therefore totally dependent on host functions for its replication. Viroid RNA is replicated by the DNA-dependent RNA polymerase of the plant host; preemption of this enzyme may contribute to viroid pathogenicity.

The RNAs of viroids have been shown to contain inverted repeated base sequences at their 3′ and 5′ ends, a characteristic of transposable elements (see Chapter 7) and retroviruses. Thus, it is likely that they have evolved from transposable elements or retroviruses by the deletion of internal sequences.

The general properties of animal viruses pathogenic for humans are described in Chapter 29. Bacterial viruses are described in Chapter 7.

PRIONS

A number of remarkable discoveries in the past 3 decades have led to the molecular and genetic characterization of the transmissible agent causing **scrapie**, a degenerative central nervous system disease of sheep. Studies have identified a scrapie-specific protein in preparations from scrapie-infected brains of sheep that is capable of reproducing the symptoms of scrapie in previously uninfected sheep (Figure 1-1). Attempts to identify additional components, such as nucleic acid, have been unsuccessful. To distinguish this agent from viruses and viroids, the term **prion** was introduced to emphasize its proteinaceous and infectious nature. The cellular form of the prion protein (PrP^c) is encoded by the host's chromosomal DNA. PrP^c is a sialoglycoprotein with a molecular mass of 33,000–35,000 daltons and a high content of α-helical secondary structure that is sensitive to proteases and soluble in detergent. PrP^c is expressed on the surface of neurons via a glycosylphosphatidyl inositol anchor in both infected and

FIGURE 1-1 Prion. Prions isolated from the brain of a scrapie-infected hamster. This neurodegenerative disease is caused by a prion. (Reproduced with permission from Stanley B. Prusiner.)

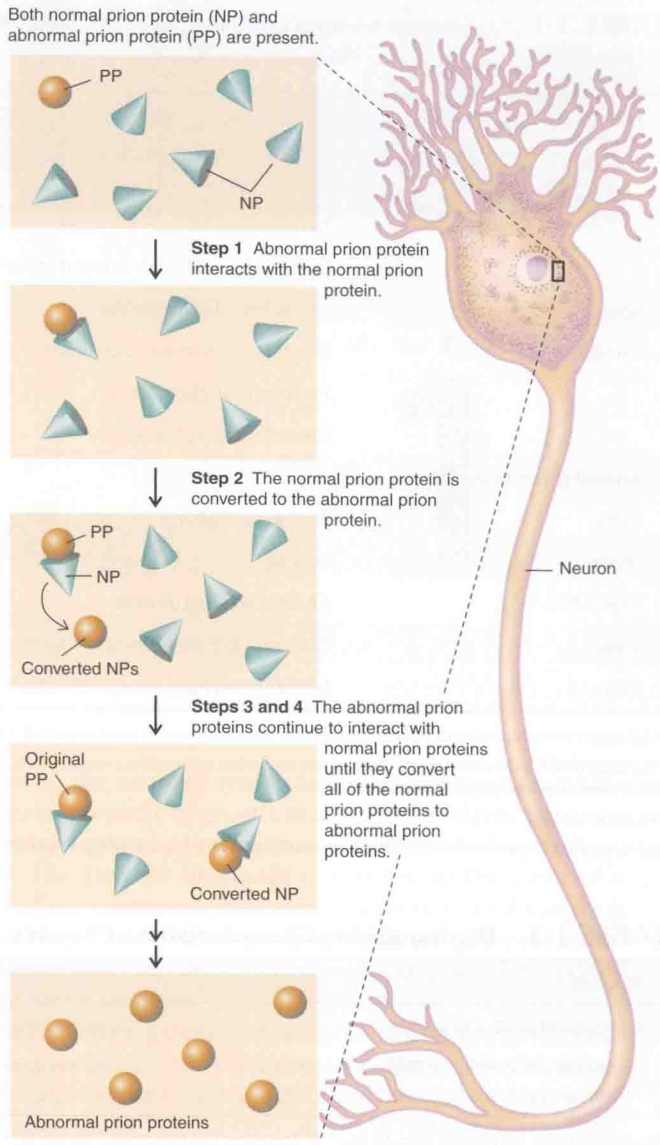


FIGURE 1-2 Proposed mechanism by which prions replicate. The normal and abnormal prion proteins differ in their tertiary structure. (Reproduced with permission from Nester EW, Anderson DG, Roberts CE, Nester MT (editors): *Microbiology: A Human Perspective*, 6th ed. McGraw-Hill, 2009, p. 342.)

uninfected brains. A conformational change occurs in the prion protein, changing it from its normal or cellular form PrP^{c} to the disease-causing conformation, PrP^{Sc} (Figure 1-2). When PrP^{Sc} is present in an individual (owing to spontaneous conformational conversion or to infection), it is capable of recruiting PrP^{c} and converting it to the disease form. Thus, prions replicate using the PrP^{c} substrate that is present in the host.

There are additional prion diseases of importance (Table 1-1 and Chapter 42). Kuru, Creutzfeldt-Jakob disease (CJD), Gerstmann-Sträussler-Scheinker disease, and fatal familial insomnia affect humans. Bovine spongiform encephalopathy, which is thought to result from the ingestion of feeds and bone meal prepared from rendered sheep offal, has been responsible for the deaths of more than 184,000 cattle in Great Britain since its discovery in 1985. A new variant of CJD (vCJD) has been associated with human ingestion of prion-infected beef in the United Kingdom and France. A common feature of all of these diseases is the conversion of a host-encoded sialoglycoprotein to a protease-resistant form as a consequence of infection.

Human prion diseases are unique in that they manifest as sporadic, genetic, and infectious diseases. The study of prion biology is an important emerging area of biomedical investigation, and much remains to be learned.

The distinguishing features of the nonliving members of the microbial world are given in Table 1-2.

PROKARYOTES

The primary distinguishing characteristics of the prokaryotes are their relatively small size, usually on the order of 1 μm in diameter, and the absence of a nuclear membrane. The DNA of almost all bacteria is a circle with a length of about 1 mm; this is the prokaryotic chromosome. Most prokaryotes have only a single chromosome. The chromosomal DNA must be folded more than 1000-fold just to fit within the prokaryotic cell membrane. Substantial evidence suggests that the folding may be orderly and may bring specified regions of the DNA